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Hope for halting autoimmune disease by turning off networks of T cell genes

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UCSF Diabetes Center researcher contributes to novel study on T cells

BY KATHLEEN JAY, UCSF Diabetes Center

As an infectious disease specialist, Dr. Alex Marson [1], M.D./Ph.D., treats patients struggling with a range of conditions that render their immune systems inefficient -- from HIV and cancer to organ transplantation.

As a scientist, Dr. Marson -- who runs a lab [2] at the UCSF Diabetes Center [3] when he's not seeing patients at UCSF Moffitt [4] or the San Francisco Veterans Affairs Medical Center [5]-- is pursuing research on ways to prevent and treat autoimmune diseases, such as type 1 diabetes [6], multiple sclerosis, rheumatoid arthritis and psoriasis.

?When treating my patients, I am again and again reminded of the central role of T cells in both infectious diseases and in autoimmune diseases, such as type 1diabetes,? Marson said.

?This provides an ongoing motivation to continue my work in the lab,? Marson added ?To decipher the molecular circuits that give these cells their unique functions.?

Using newly-identified, promising candidate drugs to target specific genes in T cells -- which drive autoimmune diseases -- Marson's research has led to new findings on how to potentially slow down the on-set of several autoimmune diseases.

These findings -- by Marson in collaboration with researchers at Harvard -- were published in the journal *Immunity* last month. The title of the article is: ?Small-Molecule ROR?t Antagonists Inhibit T Helper 17 Cell Transcriptional Network by Divergent Mechanisms [7].?

"This paper examines what makes Th17 cells -- which play a crucial role in multiple autoimmune diseases -- distinct from other closely-related T cells," Marson said.

Using a combination of genomic techniques to tease out specific mechanisms in Th17 cells of a mouse model with multiple sclerosis, Marson and his collaborators observed how lead-candidate drugs affect gene regulation in Th17 cells.

?This study was an important step because we not only identified circuits at the heart of autoimmune disease, but we also found candidate drug molecules that target these specific circuits,? Marson added.

Providing a new approach to systematically evaluate lead-candidate drugs for treating autoimmune diseases, Marson?s work provides a new vision for understanding type 1 diabetes.

?My great hope is that this approach will help to accelerate the development of new effective treatments for patients with autoimmune diseases,? Marson said.

For more information, visit:

Small-Molecule ROR?t Antagonists Inhibit T Helper 17 Cell Transcriptional Network by Divergent Mechanisms [7]

Sheng Xiao*, Nir Yosef*, Jianfei Yang, Yonghui Wang, Ling Zhou, Chen Zhu, Chuan Wu, Erkan Baloglu, Darby Schmidt, Radha Ramesh, Mercedes Lobera, Mark S. Sundrud, Pei-Yun Tsai, Zhijun Xiang, Jinsong Wang, Yan Xu, Xichen Lin, Karsten Kretschmer, Peter B. Rahl, Richard A. Young, Zhong Zhong, David A. Hafler, Aviv Regev, Shomir Ghosh, Alexander Marson?, Vijay K. Kuchroo?. Immunity. 40, 477-489 (2014).

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Links:
[1] http://diabetes.ucsf.edu/content/alexander-marson-md-phd
[2] http://marsonlab.ucsf.edu/
[3] http://diabetes.ucsf.edu/home
[4] http://www.ucsfhealth.org/
[5] http://labmed.ucsf.edu/about/hospitals/vamc.html
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